Biophysical model of coincidence detection in single Nucleus Laminaris neurons

Jonathan Z. Simon[1]
Catherine E. Carr[2]
Shihab A. Shamma[1,3]

[1]Institute for Systems Research
[2]Department of Biology
[3]Department of Electrical Engineering

University of Maryland

Supported in part by
Office of Naval Research MURI # N00014-97-1-0501
National Science Foundation # 9720334
and National Institutes of Health # DC00436

This poster is available at <http://www.isr.umd.edu/CAAR/pubs.html>

Center for Auditory and Acoustic Research

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
1999		**00-00-1999 to 00-00-1999**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Biophysical model of coincidence detection in single Nucleus Laminaris neurons	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **University of Maryland,Department of Electrical Engineering and Computer Engineering,Institute for Systems Research,College Park,MD,20742**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT **unclassified**	b. ABSTRACT **unclassified**	c. THIS PAGE **unclassified**	**Same as Report (SAR)**	**20**	

Introduction

Sound localization requires the computation of interaural time differences (ITDs) for frequencies below ~1 to 10 kHz. This is performed by binaural cells in the avian Nucleus Laminaris (NL), and its mammalian homologue, the Medial Superior Olive (MSO).

An “ITD discriminator” neuron should fire when inputs from two independent neural sources coincide (or almost coincide), but not when two inputs from the same neural source (almost) coincide. A neuron that sums its inputs linearly would not be able to distinguish between these two scenarios.

This is a biophysical model, using the program NEURON, to examine how NL neurons detect and report ITDs, their mechanisms and their limitations.

Results

- Typical chick-like parameters allow ITD discrimination up to 2 kHz.
- Typical chick-like parameters but with barn-owl-like phase locking allow ITD discrimination up to 4 kHz (can easily be pushed to 6 kHz).
- Two dendritic non-linearities aid ITD discrimination:

  1) intra-dendritic inputs sum sub-linearly.

  2) inter-dendritic interactions subtractively inhibit out-of-phase inputs.
- Response to monaural input does not require spontaneous activity from other side.
- Rate-coded ITD tuning curves convey more information than Vector-Strength-coded curves (despite/due to Vector Strength enhancement).

Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Model Description

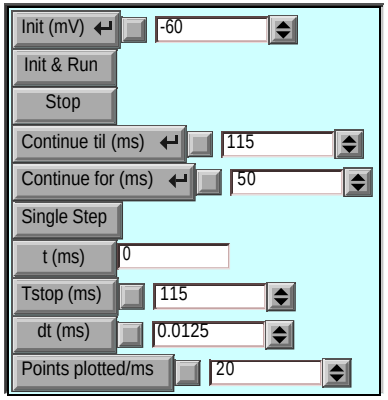
The model emulates an array of neurons, each with an adjustable number of dendrites, a soma, and an axon with an axon hillock, a myelinated segment, and a node of Ranvier. Each section has an adjustable number of equipotential compartments. All geometric, electrical, and channel parameters are adjustable, as are the number of synapses/dendrite (~ 30), the synaptic locations, and the distribution of synaptic locations. Channel types include potassium (high and low voltage activated [~Kv1.1, 1.2] and delayed rectifier), sodium, and passive. Values were obtained from physiological studies of Nucleus Magnocellularis (NM) and NL [Refs. Rathouz & Trussel, 1998, and Reyes, Rubel, & Spain, 1996]. Voltage dependent channels are specified by Hodgkin-Huxley-like parameters. Each neuron in the array feeds into a single inhibitory neuron, which feeds back onto all neurons in the array.

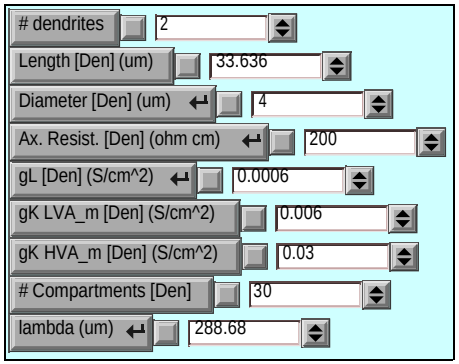
The stimulus is a pure tone of adjustable frequency, with adjustable interaural phase difference (or contralateral monaural stimulus with variable ipsilateral spontaneous activity). More complex stimuli can be easily introduced.

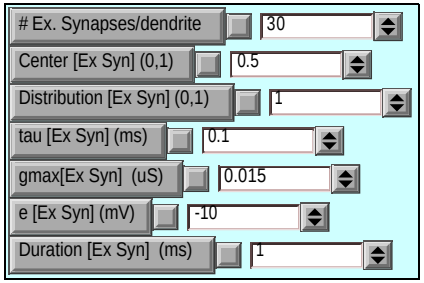
The synapses fire with conductance proportional to an alpha-function, with adjustable time constant, peak conductance, and reversal potential. The excitatory synapses fire as individual Poisson processes, with probability rate given by a modified sinusoid, with adjustable amplitude and vector strength. The inhibitory neuron is a simple integrate-and-fire type.

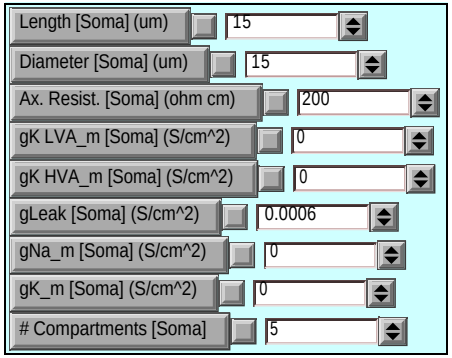
The implementation uses the program NEURON and has a graphical user interface for controlling the parameters and running the model. NEURON provides a real-time display of data and analysis including the potential at various locations, the two stimuli, the synaptic firings, spike counters, period histograms of synaptic firings and the action potentials, and their vector strengths.

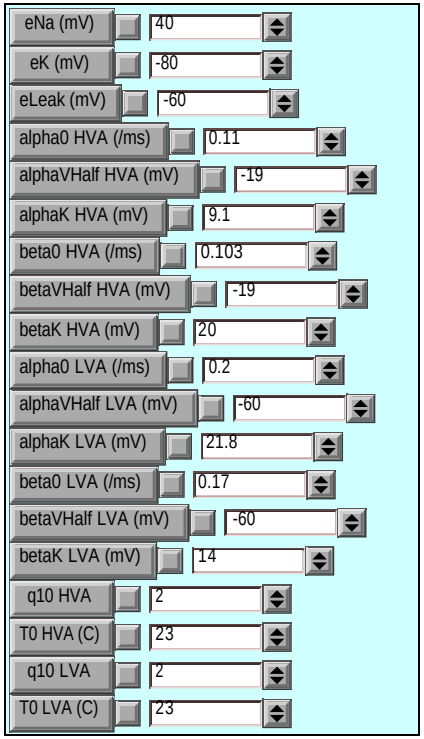
NEURON Panels

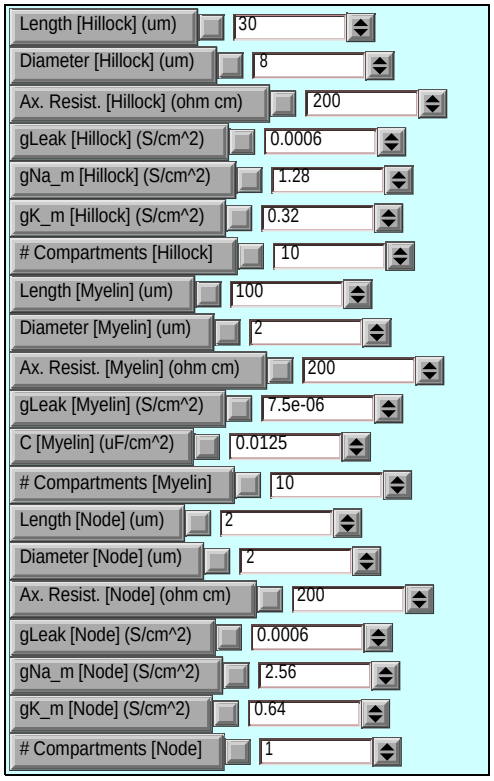


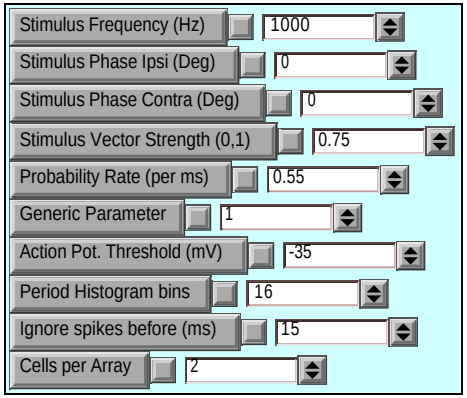


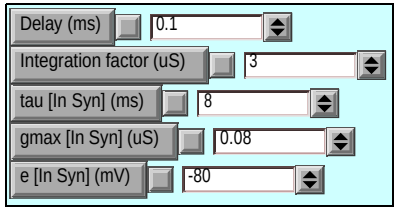


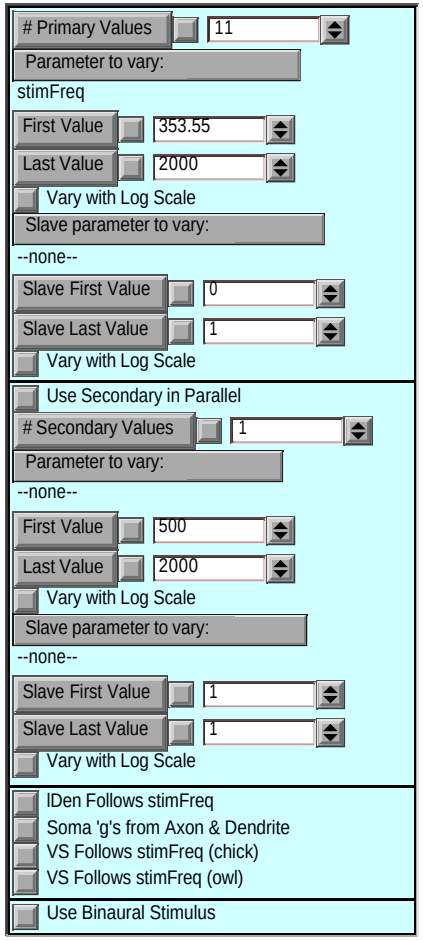










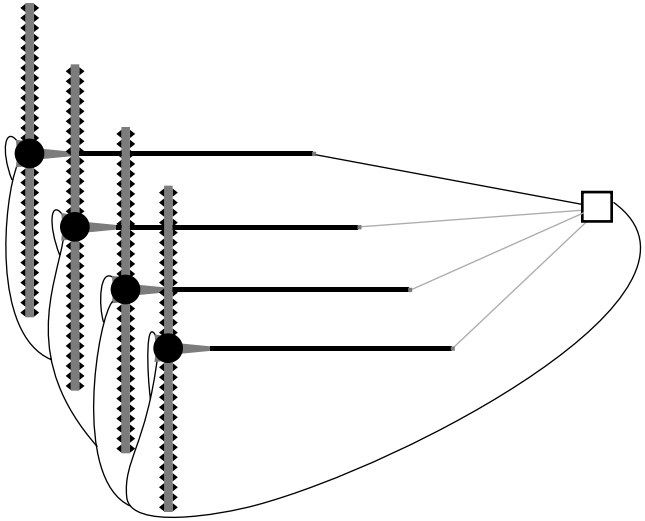


Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

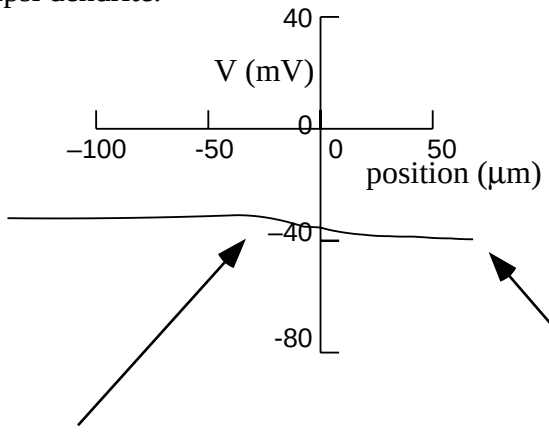
Geometry & Connectivity

A typical model cell has 2 - 8 dendrites, each 20 - 400 μm long and 2 - 4 μm in diameter, a spherical soma of diameter 15 μm, and an axon. Each dendrite has ~30 excitatory synapses. The axon has an axon hillock, a segment with myelination, and a node of Ranvier. The output feeds into an integrate-and-fire inhibitory cell which feeds back to all cells in the array.

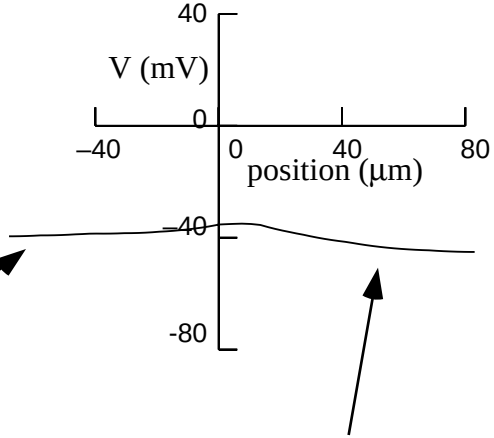


Spatial intracellular potential plots

Down the axon, through the soma, and down along the ipsi dendrite.



The potential up the ipsi dendrite, through the soma, and down along the contra dendrite.



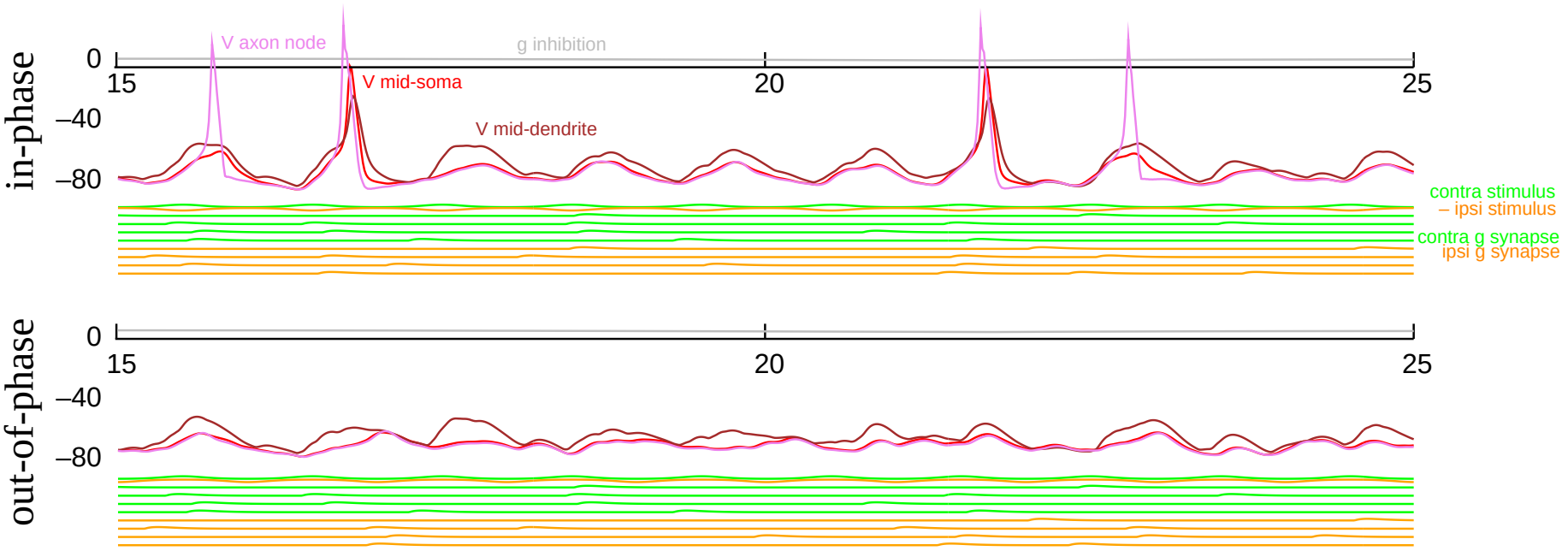
Axon hillock initiating spike from ipsilateral current surge, despite contralateral current drain

Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Time Plots

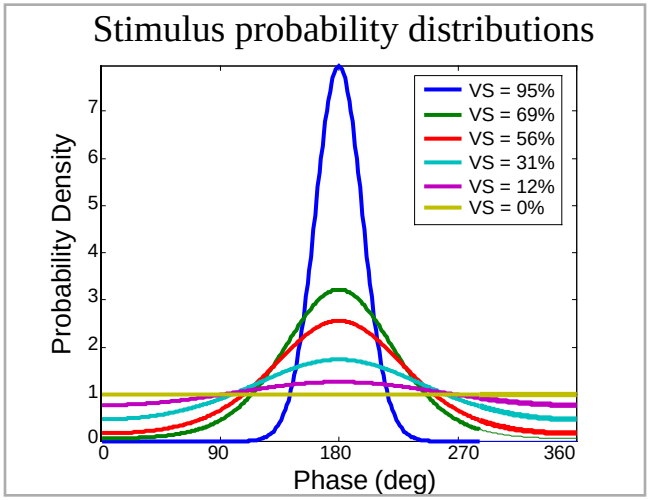
A pair of cells receives the same stimulus probability distributions (here, f =1 kHz).
The top receives its inputs binaurally in-phase, and the bottom out-of-phase.



Red tracks the intracellular potential in mid-soma, magenta at the axon tip, and brown in one dendrite. Gray plots inhibitory conductance.

Directly beneath are the pair of presynaptic stimulus probability distributions. See figure to right for other examples of stimulus probability distributions. →

The bottom 8 curves of each graph show realized synaptic currents (note spread from Poisson distribution).

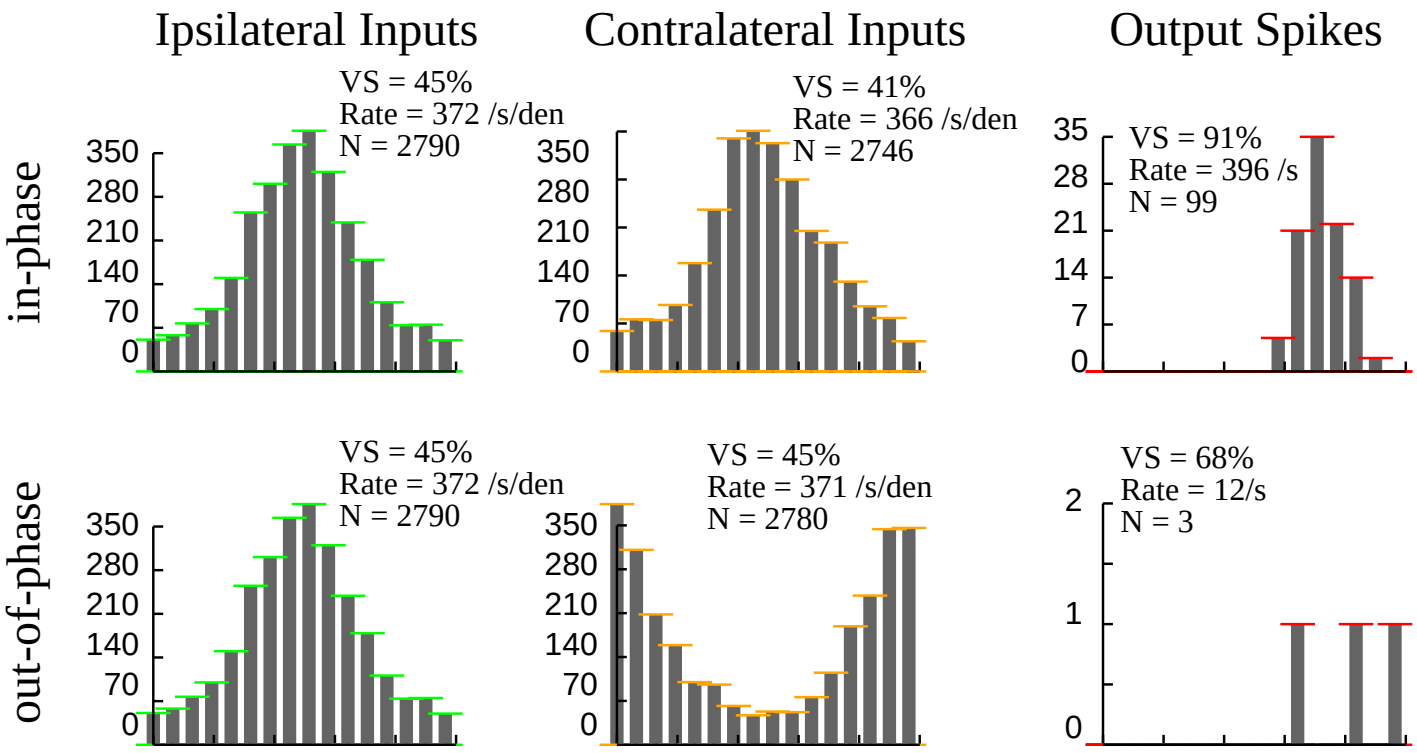


Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Period Stimulus Histograms

The same pair of cells (and stimulus), tracked for 250 ms:



Vector Strength (VS) measures phase locking, between 0 and 100%.

The in-phase-stimulus cell increased VS over its inputs (a little too well).

Parameter Space

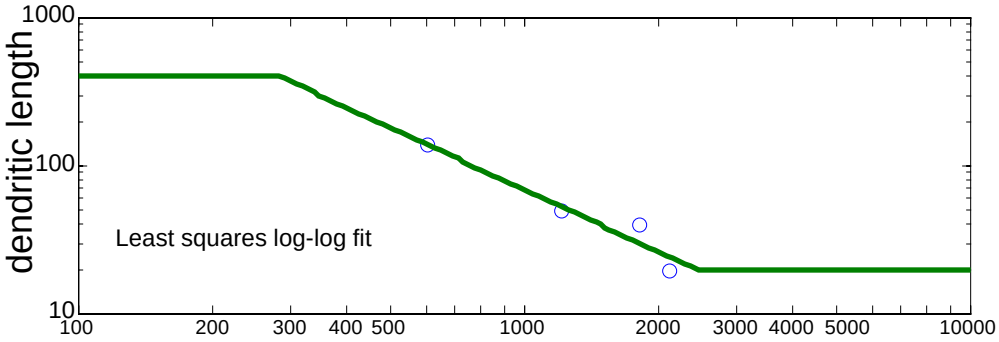
The dimensionality of the parameter space is high, with only a small region biologically relevant.

To limit the search through parameter space, most trials compare a pair of identical cells receiving identical stimuli, but one in-phase and the other out-of-phase. Trials using monaural stimulus do not need pairs.

Most trials co-vary the dendritic length and stimulus vector strength with the stimulus frequency, using experimentally derived relations.

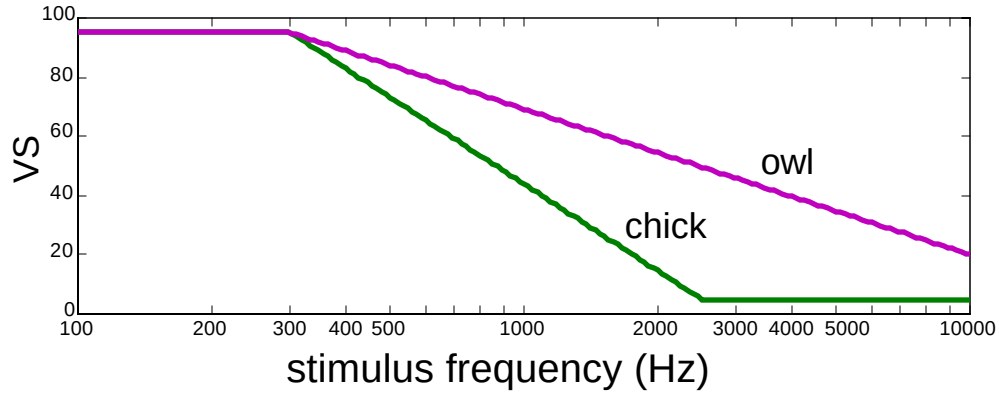
A linear fit between log(*dendritic length*) and log(*best frequency*)

Data from Smith & Rubel, 1979.

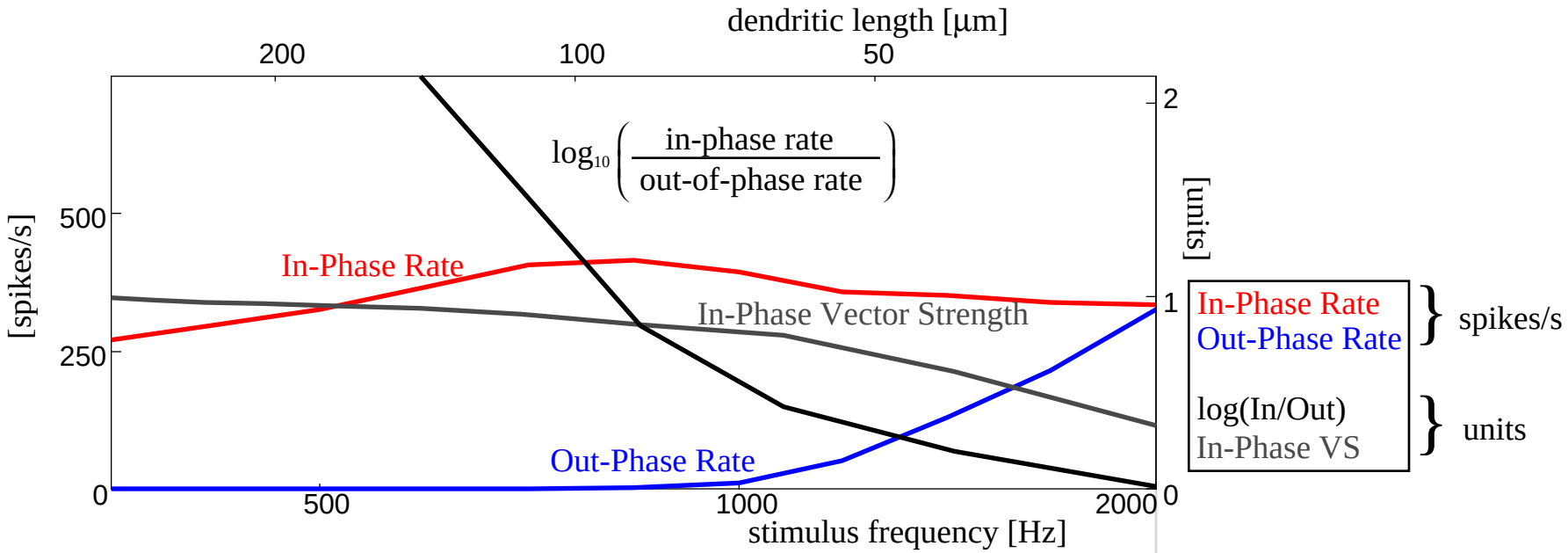


A linear fit between *vector strength* and log(*best frequency*)

Data from Köppl, 1997, Warchol & Dallos, 1990.

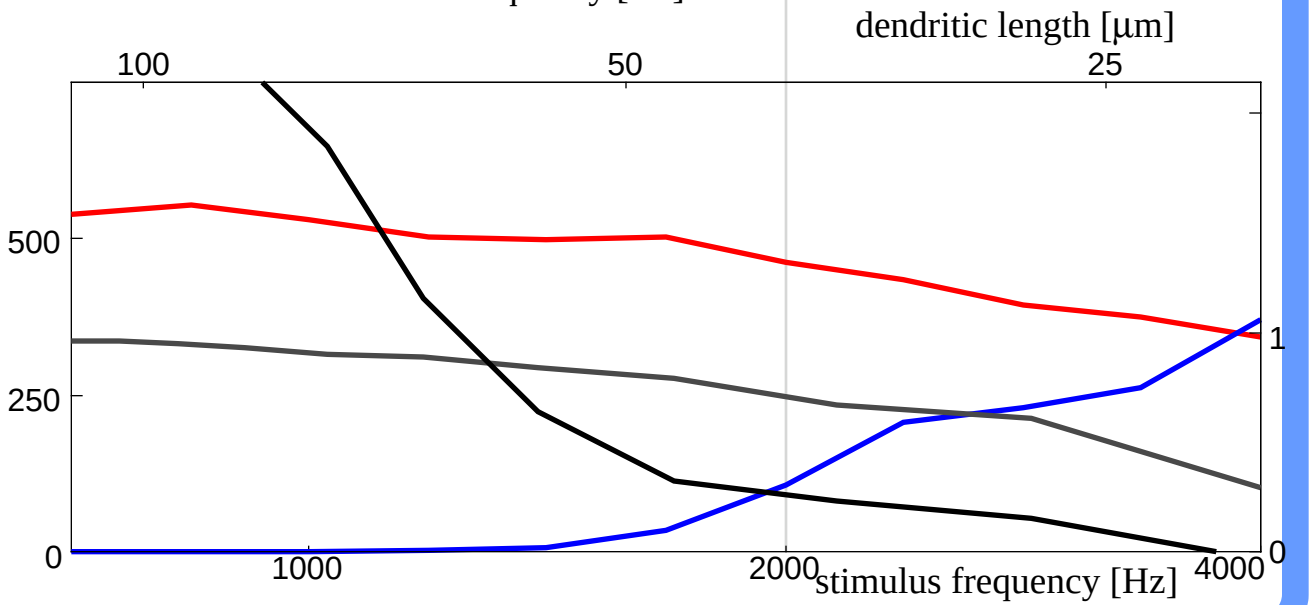


ITD Discrimination



Good ITD discrimination (high ratio) until ~2 kHz.

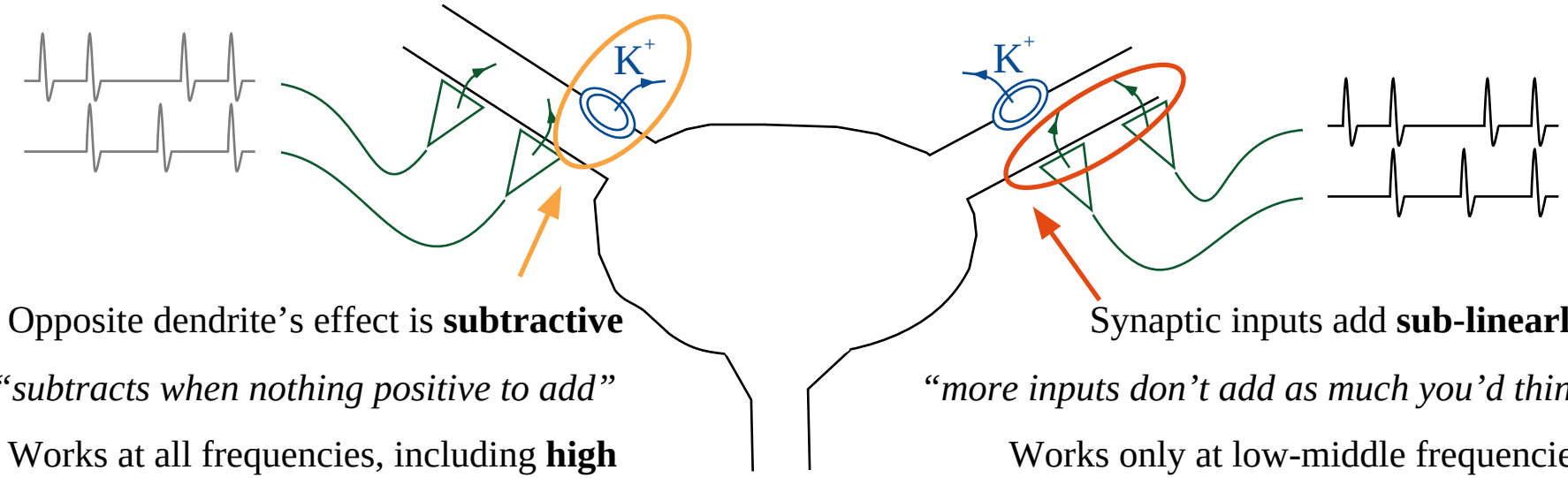
At right, keeping all parameters the same, but using Barn Owl vector strength gives good ITD discrimination until ~4 kHz. (One can go up to ~6 kHz simply by adding more dendrites.)



Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Non-Linearities



Opposite dendrite's effect is **subtractive**

"subtracts when nothing positive to add"

Works at all frequencies, including **high**

Synaptic inputs add **sub-linearly**

"more inputs don't add as much you'd think"

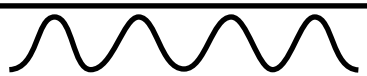
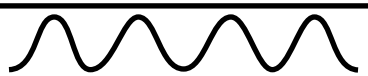
Works only at low-middle frequencies

New result

Found by Agmon-Snir et al.

Both effects prevent many inputs from right side wrongly causing cell to fire without inputs from the left side.

Reduction in "false positives"

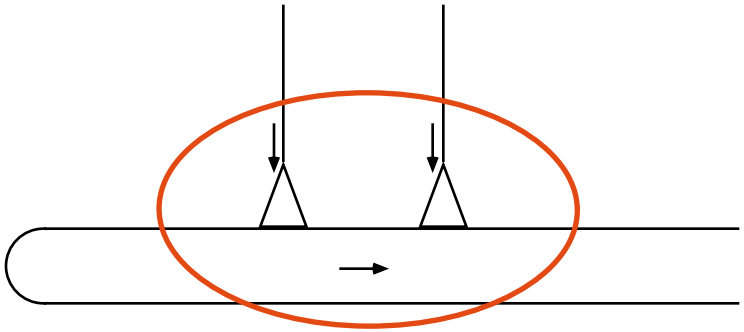
Firing Rates	**with non-linearities**	**without non-linearities**
In-Phase		
Out-of-Phase		 too many false positives

Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Intra-Dendritic Sub-Linearity

EPSCs from the excitatory synapses sum sub-linearly on entering the dendrite.



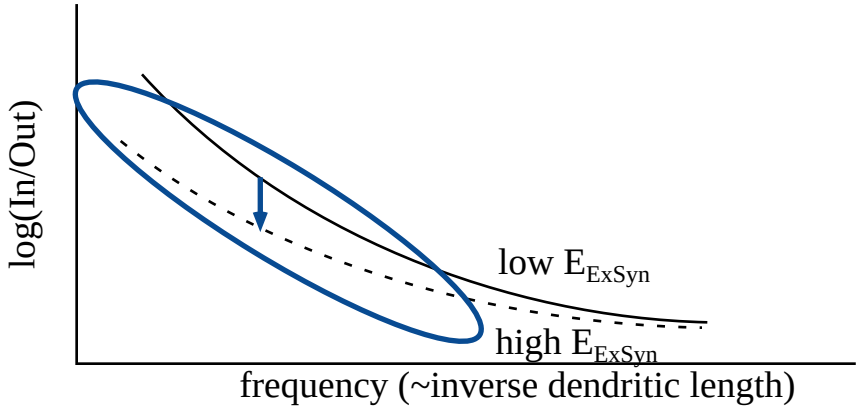
synapses a	synapses b	dendritic result
1	0	1
0	1	1
1	1	1.5

This non-linearity arises from a low synaptic reversal potential (E_{ExSyn}).

$$I_{\mathrm{ExSyn}} \propto (V - E_{\mathrm{ExSyn}})$$

Concurrent EPSCs raise the potential V, diminishing the effect of each EPSC. At the extreme, if $V > E_{ExSyn}$, PSCs are effectively inhibitory.

The effect is strongest for longer dendrites (i.e. more electrically isolated).



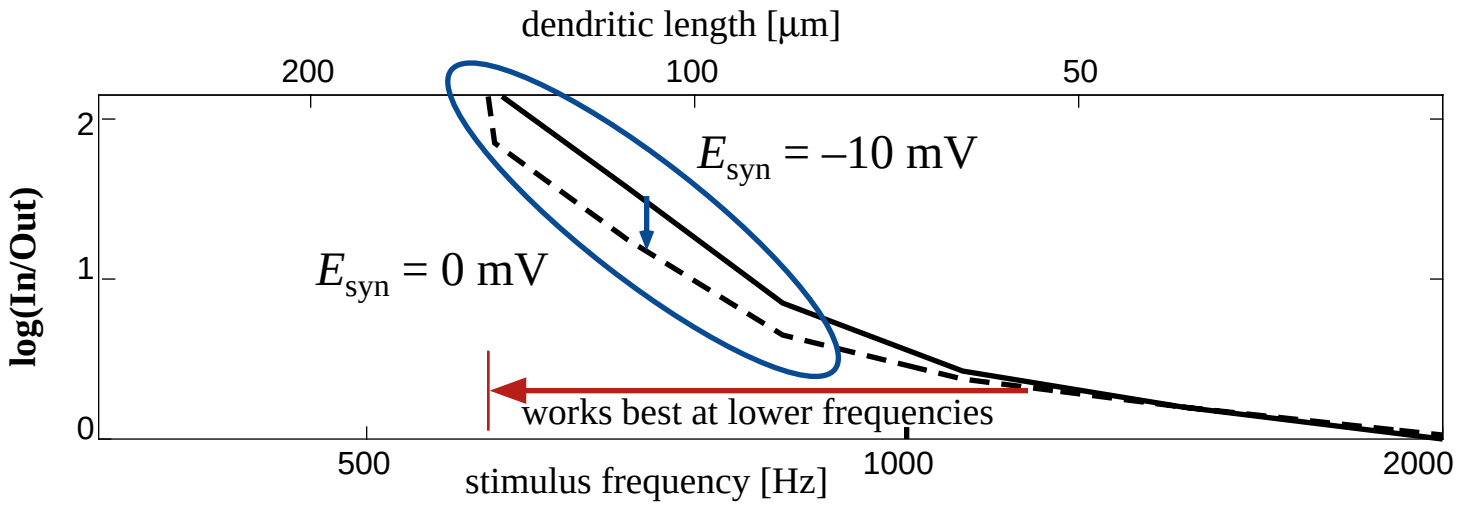
See Agmon-Snir, et. al. 1998

(Synaptic depression is another example of a sub-linearity.)

Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

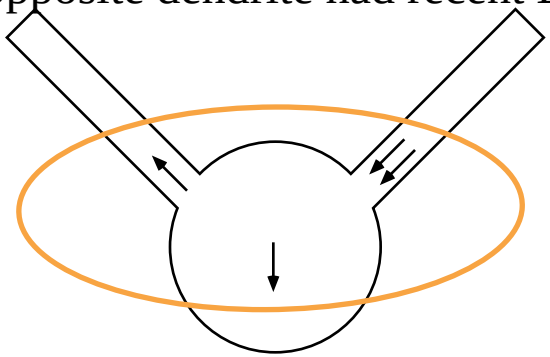
Sub-Linearity Results



- Shifting the synaptic reversal potential upwards reduces the sub-linearity, worsening the ratio of in-phase/out-of-phase firing rates.
- The effect is present only at lower frequencies.

Inter-Dendritic Subtraction

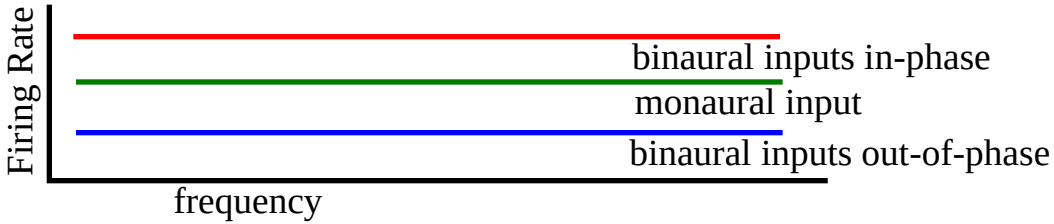
Current flowing into the soma from dendritic EPSPs is subtracted by the opposite dendrite (if without its own EPSPs). The subtraction is greater when the opposite dendrite had recent EPSPs.



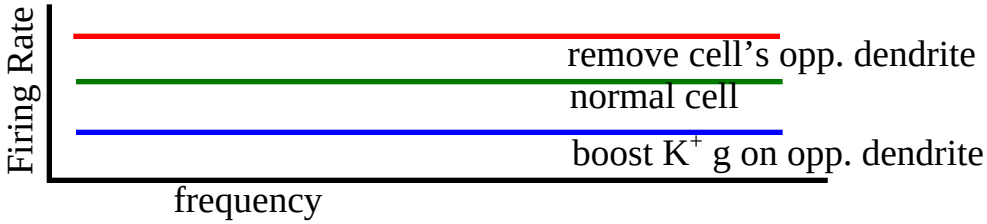
dendrites a	dendrites b	somatic result
1	0	> 0.5
0	1	> 0.5
1	1	> 2

This non-linearity arises from voltage-dependent K^+ channels. When there are no ESPSs in the opposite dendrites, the channels are somewhat activated, acting as a mild current sink. When there were recent ESPSs in the opposite dendrite, the channels are strongly activated, acting as a large current sink.

This gives a hierarchy of firing rates for different stimuli:



Another hierarchy, for all the same *monaural stimulus* but for different cells:



It is present at *all* frequencies.

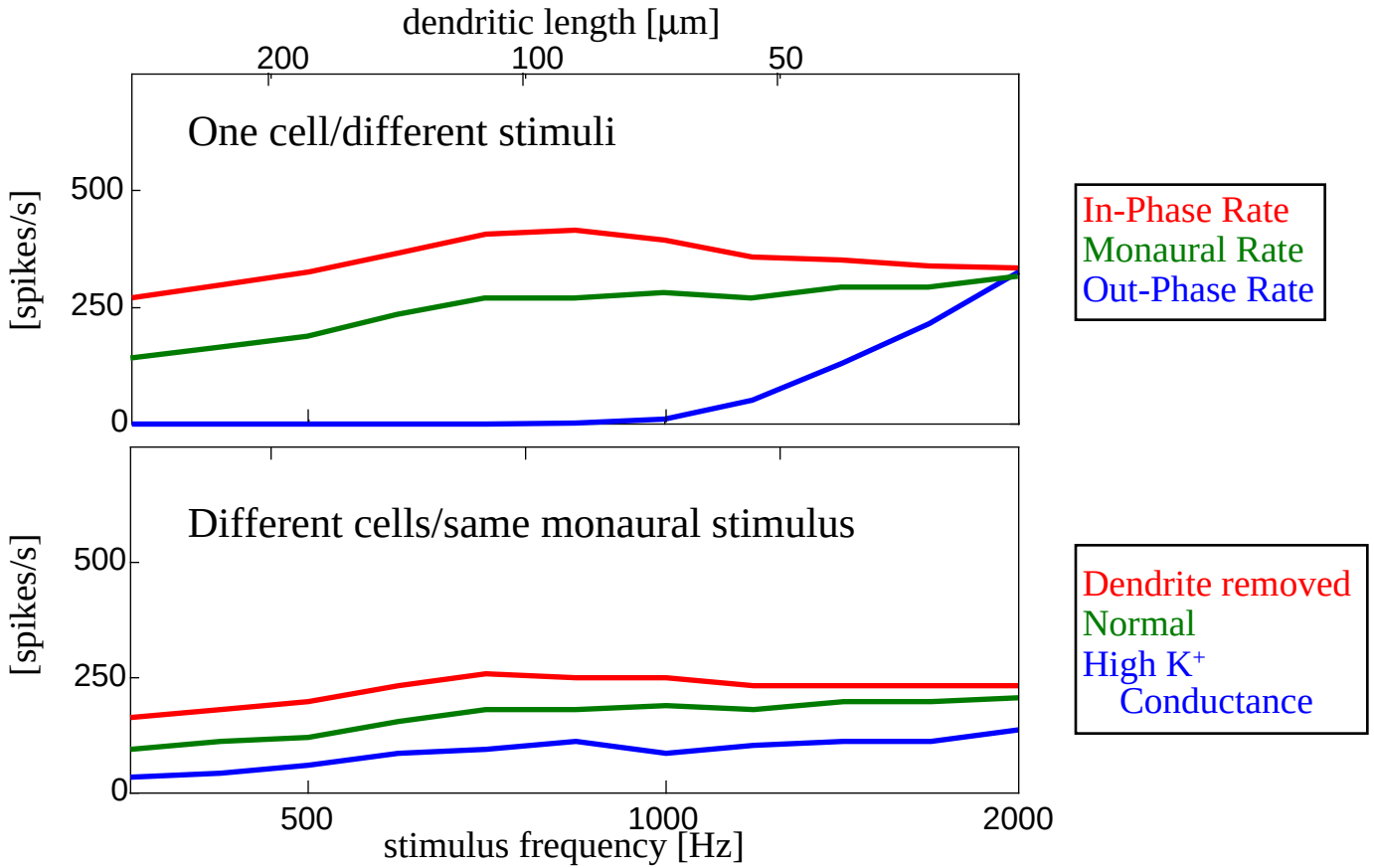
Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Subtraction Results

The out-of-phase rate is suppressed relative to the monaural rate.

The opposite dendrite acts as a current sink.



Note that the cells fire well with *no* stimulus on the opposite side. The cell is not just a coincidence detector, it is an ITD discriminator: it does not need spontaneous activity on the opposite side in order to fire.

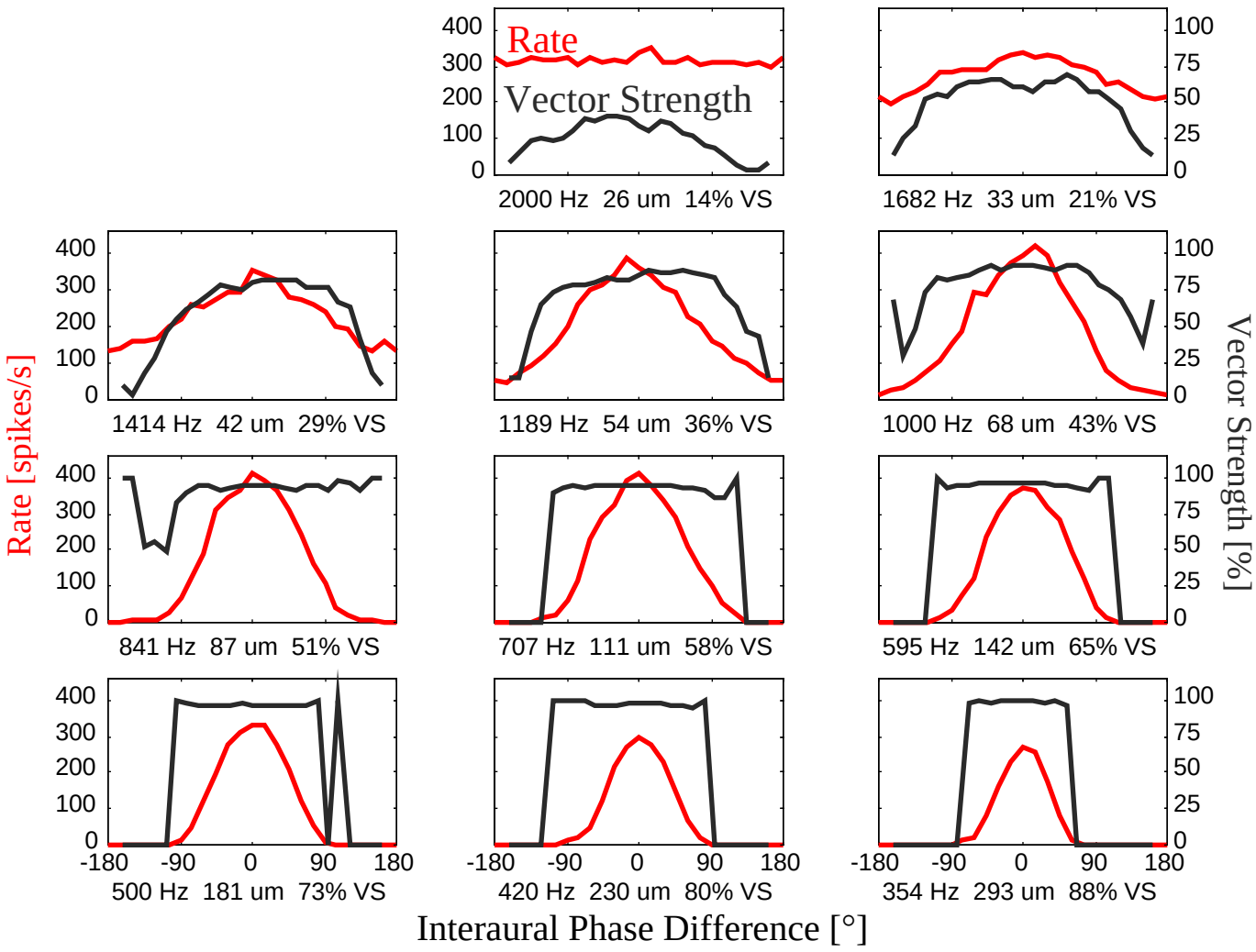
The effect is present at all frequencies.
(The meeting of in- and out- rates at ~ 2kHz is a consequence of poorly phase-locked inputs.)

Phase Locking

The responses to a 360° range of phase difference give ITD tuning curves (Interaural Phase Difference + frequency gives ITD)

Rate coding and vector-strength coding give two separate ITD tuning curves.

The “rate” ITD curves are more sharply tuned than the “vector-strength” ITD curves (note that the vector strength is not reliable when the firing rate is low).



Parameters used were not tuned to give the most accurate possible results. These results show 1) an over-enhancement of output VS over the input VS, making the VS-coded ITD tuning curves appear extra flat, and 2) an over-suppression of rates for nearly out-of-phase inputs, which makes the rate-coded ITD tuning curves look extra sharp (compared to experiment)

Center for Auditory and Acoustic Research

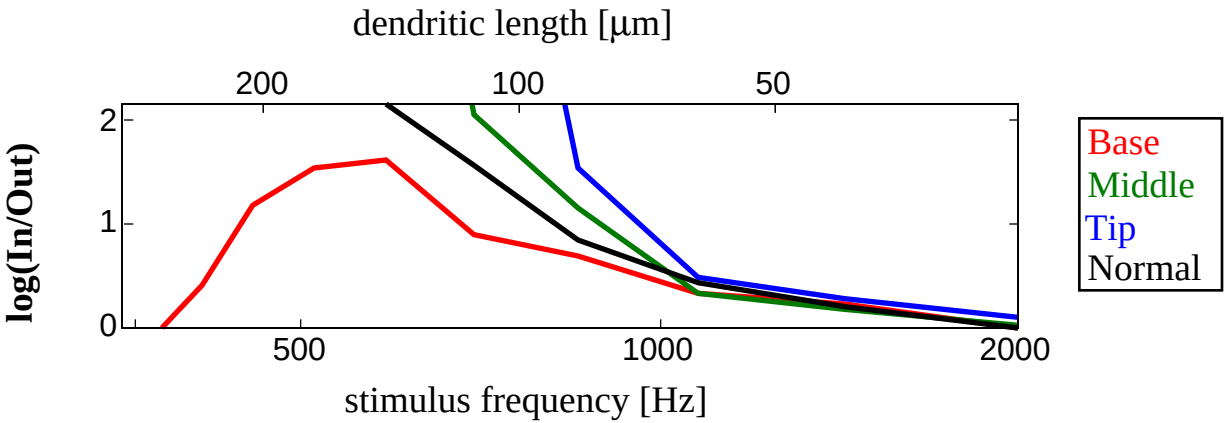
Institute for Systems Research
University of Maryland

Synaptic Location

There are many "experiments" one can do with a model that are either difficult or fundamentally impossible in the laboratory.

In this case we compare In-Phase/Out-of-Phase ratios for 3 interesting but "impossible" scenarios.

In all but the black (normal) case, every excitatory synapse on each dendrite has been put at the same point. In the 3 colored cases, they are all at the dendrite base, dendrite center, and dendrite tip.



The only difference is for long dendritic lengths/low frequencies, as expected, since the intra-dendritic non-linearity requires an electrically isolated dendrite.

Base:
The intra-dendritic non-linearity is diminished, the out-of-phase rate goes up (the number of false positives goes up), and the In-Phase/Out-of-Phase ratio goes down.

Middle & Tip:
The more isolated the synapses from the soma, the higher the effect of the intra-dendritic non-linearity, and the more the In/Out ratio goes up.

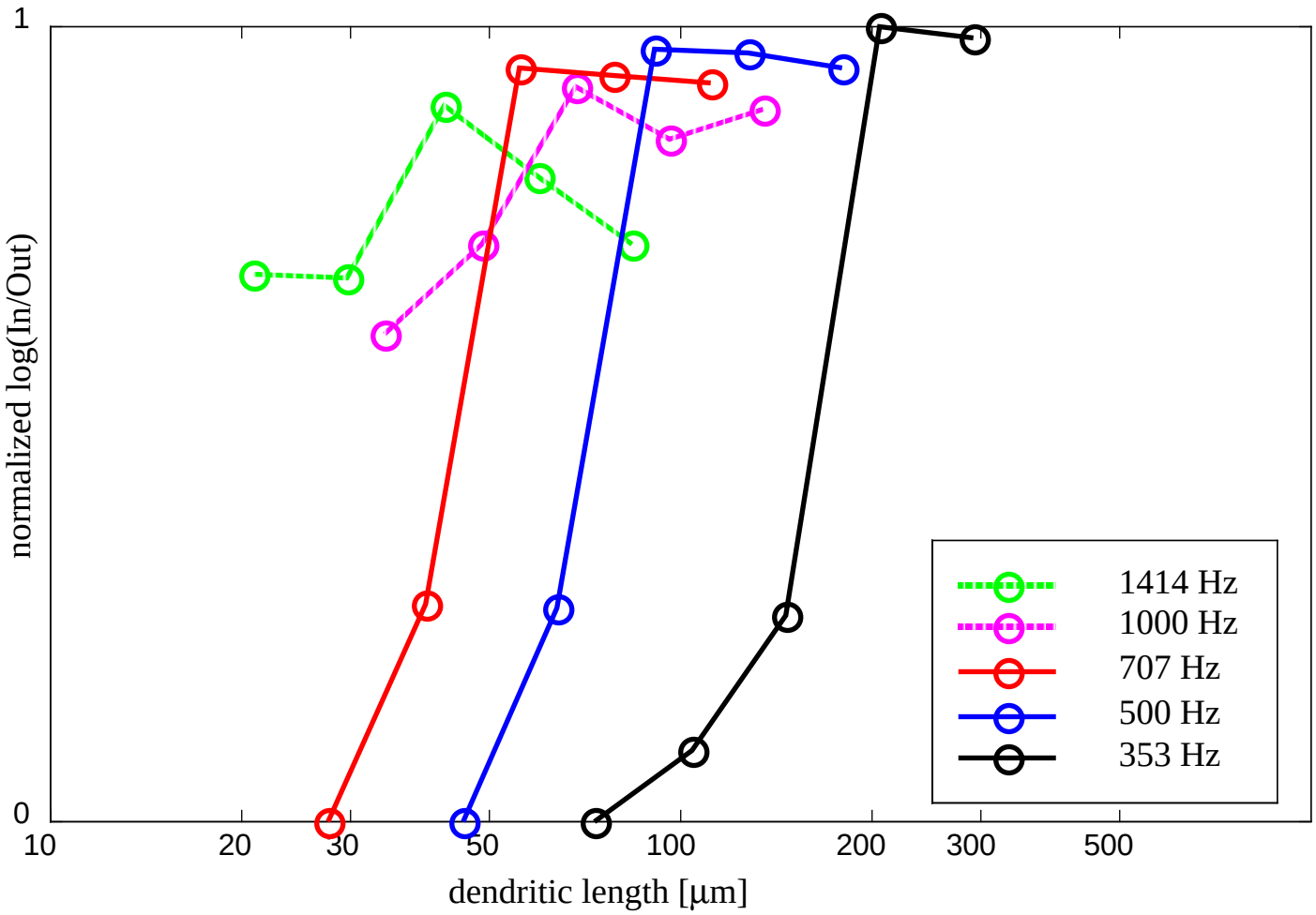
Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Dendritic Length

The Intra-dendritic sublinearity leads to an optimal dendritic length, as shown by Agmon-Snir et al.

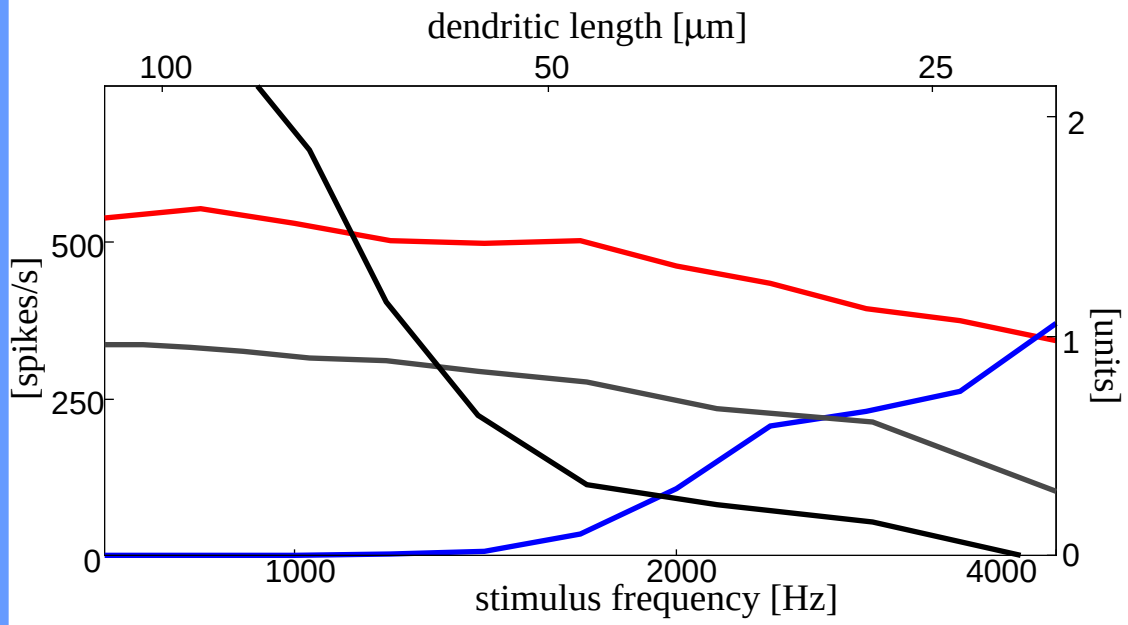
For every stimulus frequency there is a dendritic length, longer than which, performance no longer increases. The effect is most pronounced at lower frequencies.



Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

ITD Discrimination—Barn Owl

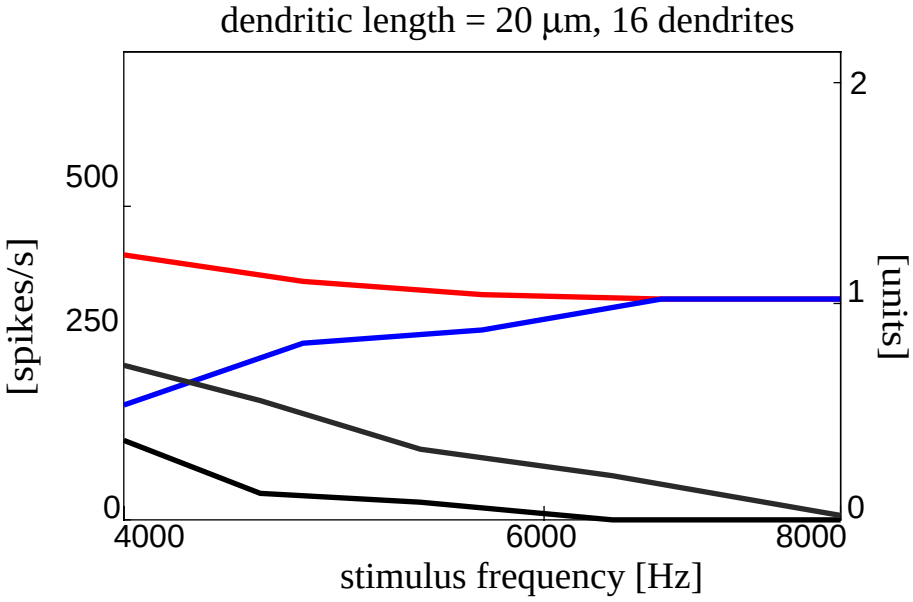


In-Phase Rate
Out-Phase Rate

log(In/Out)
In-Phase VS

The top plot shows ITD discrimination using chick-like parameters, but merely increasing the vector-strength to that of the barn owl.

The right plot shows ITD discrimination going up to ~6 kHz by simply adding more dendrites.



Center for Auditory and Acoustic Research

Institute for Systems Research
University of Maryland

Selected References

"A Dendritic Model of Coincidence Detection in the Avian Brainstem," J. Z. Simon, C. E. Carr and S. A. Shamma, to appear in Neurocomp. 1999.

"The Role of Dendrites in Auditory Coincidence Detection," H. Agmon-Snir, C. E. Carr, and J. Rinzel, Nature **393**, 268-272 (1998).

"The NEURON Simulation Environment," M. L. Hines and N. T. Carnevale, Neural Computation **9**, 1179-1209 (1997). See also <http://www.neuron.yale.edu>.

"Organization and Development of Brain Stem Auditory Nuclei of the Chicken: Dendritic Gradients in Nucleus Laminaris," D. J. Smith and E. W Rubel, J. Comp. Neur. **186**, 213-240 (1979).

"*In Vitro* Analysis of Optimal Stimuli for Phase-Locking and Time-Delayed Modulation of Firing in Avian Nucleus Laminaris Neurons," A. D. Reyes, E. W. Rubel, and W. J. Spain, J. Neurosci. **16**, 993-1007 (1996).

"A Circuit for Detection of Interaural Time Differences in the Brain Stem of the Barn Owl," C.E. Carr and M. Konishi, J. Neurosci. **10**, 3227-3246 (1990).

"Characterization of Outward Currents in Neurons of the Avian Nucleus Magnocellularis," M. Rathouz and L. Trussel, J. Neurophysiol. **80**, 2824-2835 (1998).

"The Role of GABAergic Inputs for Coincidence Detection in the Neurones of Nucleus Laminaris of the Chick," K. Funabiki, K. Koyoano, and H. Ohmori, J. Physiol. **508.3**, 851-869 (1998).

"Neural Coding in the Chick Cochlear Nucleus", M. E. Warchol and P. Dallos, J. Comp. Physiol. A **166**, 721-734 (1990).

"Phase Locking to High Frequencies in the Auditory Nerve and Cochlear Nucleus Magnocellularis of the Barn Owl, *Tyto alba*," C. Köppl, J. Neurosci. **17**, 3312-3321 (1997)